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572-339

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

Subject: EPA Registration Numbers: 572-336 thru 572-339;
Data Submitted In Support Of IBA RED (Batch 1).

From: Van M. Seabaugh V.M.Seabaugh 9.21.94
Precautionary Review Section (PRS)
Registration Support Branch
Registration Division (7505W)

To: Cynthia Giles-Parker (PM 22)
Herbicide-Fungicide Br.
Registration Division (7505C)

Registrant: Rockland Corp.
686 Passaic Ave.
West Caldwell, N.J. 07007

Ingredients (From Labels; 12-28-92)

EPA Reg. No. 572-336

Active Ingredient
Indole-3-butyric acid.....4.40%
Inert Ingredients.....95.60%

EPA Reg. No. 572-337

Active Ingredient
Indole-3-butyric acid.....1.0%
Inert Ingredients.....99.0%

EPA Reg. No. 572-338

Active Ingredient
Indole-3-butyric acid.....2.0%
Inert Ingredients.....98.0%

EPA Reg. No. 572-339

Active Ingredient
Indole-3-butyric acid.....3.0%
Inert Ingredients.....97.0%

Background Information

The PRS was asked to review acute toxicity studies (§81-1 thru §81-5; MRID Numbers 431902-1 thru -05).

Summary

Study	MRID #	Results	Toxicity Category	Classification
Oral Toxicity	431902-1	Limit test; 5 g/kg; 0/10 mortality (5♂, 5♀)	IV	Guideline
Dermal Toxicity	431902-2	Limit test; 2 g/kg; 0/10 mortality (5 ♂, 5 ♀)	III	Guideline
Inhalation Toxicity	421902-3	Limit test; 0/10 mortality (5♂, 5♀)	III	Guideline
Eye Irritation	431902-4	*	III	Guideline
Dermal Irritation	431902-5	P.I.I.= 0.1 for 1, 24, 48, & 72-hr. observations	IV	Guideline
Dermal Sensitizatom	--	Study not submitted. Registrant should submit data or request waiver	--	--

*: No positive scores for opacity or iritis for observations at 1, 24, 48, 72 hours & day 4. Positive scores for conjunctivae (at least one of the 3 measurements) 6/6 for hours 1, 24, 48; 2/6 at 72 hrs.; 0/6 at 4 days [PRS Note: Lab should be told to report animal weights in future submissions.

DATA REVIEW FOR ACUTE ORAL TOXICITY TESTING (§ 81-1)

Product Manager: Cynthia Giles-Parker (PM 22)
Reviewer: Van M. Seabaugh
MRID No.: 431902-1
Report Date: 2-15-94
Report Title: HORMO Root 4 - EPA Reg. No. 572-336, Lot No. 013233.
Testing Facility: Product Safety Labs, 725 Cranbury Road, East Brunswick, N.J. [EPA Acute Oral Toxicity Test].
Report No.: T-2780
Author(s): Ralph Shapiro, Ph.D.
Species: Sprague-Dawley Rats
Weight: 192-212 grams
Source: Hilltop Lab Animals, Scottdale, PA
Test Material: HORMO Root 4 (EPA Reg. No. 572-336, lot 013233). White powder; 40% w/w suspension in a 2% w/w suspension of carboxymethylcellulose (CMC) in distilled water.
Quality Assurance (40 CFR §160.12): Statement submitted.
Conclusions:

- A limit test was conducted (5♀, 5♂) at 5 g/kg. No mortality was reported for the 14-day observation period. No significant listings were reported at gross necropsy or during the 14-day observations.
- The estimated LD_{50} is > 5 g/kg.
- Toxicity Category: IV.
- Classification: Guideline.

Procedure: Young, adult Sprague-Dawley rats (5 males, 5 females) were fasted (approximately 19 hours) before dosing by gavage with 5 g/kg of the product [40% (w/w) suspension in a 2% (w/w) suspension of CMC in distilled water]. The observation period was 14 days.

Results:

Dosage	(Number Killed/Number Tested)		
	Males	Females	Combined
5 g/kg	0/5	0/5	0/10

Symptoms & Gross Necropsy Findings. No significant listings were reported at gross necropsy or during the 14-days observations.

DATA REVIEW FOR ACUTE DERMAL TOXICITY TESTING (§81-2)

Product Manager: Cynthia Giles Parker (PM 22).
Reviewer: Van M. Seabaugh.
MRID No.: 431902-2.
Report Date: 3-24-94.
Report Title: HORMO Root 4 - EPA Reg. No. 572-336, Lot No. 013233. [EPA Acute Dermal Toxicity Test].
Laboratory: Product Safety Labs, 725 Cranbury Road, East Brunswick, N.J.
Report No.: T-2783.
Author: Ralph Shapiro, Ph.D.
Species: Sprague-Dawley rats
Weight (grams): Males (262-297); females (210-268).
Source: Hilltop Lab Animals, Scotdale, PA.
Test Material: HORMO Root 4- EPA Reg. No. 572-336, Lot No. 13233; white powder
Quality Assurance (40 CFR §160.12): Statement submitted.
Summary:

This study is assigned a toxicity category III (Classification: core - guideline). It is assumed that the "boiler plate" statement on page 9 is in error mentioning "rabbits", and that rats, as mentioned throughout the rest of the text, were tested.

Procedure:

"Approximately 18.5 hours before application, five male and five female rats were prepared by clipping the skin free of hair over the dorsal and lateral surfaces from scapular to pelvic area. The test sites of all animals were abraded with a needle prior to application of the test substance. **[PRS Comment: The EPA Guidelines lists an unabraded test site, and an abraded test site was used here. However, it is being allowed by the PRS, because it should produce a more severe response with the anticipated easier dermal penetration of the test substance].** Two thousand mg/kg of the test substance was moistened with distilled water (1 ml of distilled water per 1 g of test substance) and applied evenly over a dose area of approximately 4 x 6" (approximately 10% of the body surface) and covered with a 2 x 2" adhesive-backed gauze patch. The patch and entire trunk of each rat were then wrapped with 2" Durapore tape to aid in maintaining test patch position and to minimize evaporation. After 24 hours of exposure to the test substance, the patches were removed and the test sites were gently wiped clean of any residual test substance using water and a clean towel. The rats were observed for gross toxicity and mortality 1, 2.5, 5, 23, and 24 hours after test substance application. Thereafter, they were observed at least once daily for the remainder of the 14 day test period."

Results:

Reported Mortality

DOSAGE	(NUMBER KILLED/NUMBER TESTED)		
	Males	Females	Combined
2 g/kg	0/5	0/5	0/10

Symptoms & Gross Necropsy Findings: Observations (in-life) included yellow discoloration of dose site, erythema, and edema. Necropsy observations reported were "moderately red' lungs with all other tissues/organs reported as "appear normal."

DATA REVIEW FOR ACUTE INHALATION TOXICITY TESTING (§81-3)

Product Manager: Cynthia Giles-Parker (PM 22)
Reviewer: Van M. Seabaugh
MRID No.: 431902-3
Report Date: 3-7-94
Testing Facility: Product Safety Labs, 725 Cranbury Road, East Brunswick, N.J.
Report Title: EPA Acute Inhalation Limit Test

Report No.: T-2785
Author: Gary Wnorowski, B.A.
Species: Sprague Dawley rats
Weight: 204-222 g (females); 213-244 g (males).
Source: Hilltop Lab Animals, Scottdale, PA
Test Material: Hormo Root 4; EPA Reg. No. 572-336; lot 13233; white powder.
Quality Assurance (40 CFR §160.12): Signed statement submitted.
Summary:
The study is classified as Toxicity Category IV (Guideline).
Procedure:

Pretesting
"Prior to initiation of the full inhalation study, pre-test trials were conducted to establish procedures for achieving as closely as possible the desired (5 mg/liter) or highest possible chamber concentration and desired particle size distribution (≥50% of particles <3 microns and 25% of particles <1 micron). In these trials the following adjustments were made in an attempt to achieve these objectives: 1) Pressure (PSI): varied. 2) Compressed air flow: varied. 3) Room air flow: varied. 4) Total air flow: varied. 5)

Motor setting: varied. 6) Dust generating system: constant. 7) Packing pressure: varied. 8) Material preparation: varied. The procedures and aerosolization equipment used in the full test were based on results of pre-test Trial #14. This provided a chamber concentration of 2.10 mg/liter and a particle size distribution of 40.9% ≤ 3.3 microns and 5.0% ≤ 1.1 microns. The test substance used in trail # 14 (as well as the full test) was ground for 24 hrs in a ball mill prior to aerosolization. During preliminary testing, it was established that the time of grinding which produced an aerosol of proper concentration with the most desirable particle size distribution was 24 hours. Attempt at aerosol generation using the material as received (unground) or ground for shorter periods (1 and 3 hours) returned inferior particle size distributions and exceptionally low chamber concentrations."

Main Test

"Five rats of each sex were exposed to the test atmosphere for 4 1/2 hours at a gravimetric chamber concentration of 2.02 mg/L. Chamber concentration and the particle size distribution of the aerosolized test substance were determined periodically during the exposure period."

"The exposure chamber, air supply and equipment used to measure particle size distribution, air flow calibration and chamber concentration are described.

Exposure Chamber Rectangular perspex chamber with a volume of 100 liters operated under sight negative pressure.

Air Supply Approximately 30 liters per minute (lpm) supplied from a compress gas cylinders of breathing grade air (Arco, Dry Air) to the Wright Dust Generator. Approximately 30.6 lpm of filtered conditioned room air was supplied as diluent air.

Ambient Conditions The room temperature and humidity ranges during exposure were 70-71° F and 40-48 % RH, respectively. The temperature and relative humidity range within the exposure chamber was 70-72° F and 45-48% RH. Room conditions and in-chamber measurements were made with a Taylor Humidiguide, Model #5502.

Test Substance Preparation Approximately 1.4 kg of the test substance was processed in a urethane-line milling jar (1.6 gallons Abbthane, Paul O'Abbe) with porcelain grinding media (0.5" balls) for 24 hours. After milling, the substance as sieved through a screen (Tyler) to separate it from grinding media and any other large particles which remained.

Dust Generation The test substance was packed into the DF 183 Wright Dust Container and compressed to

3,500 lbs/in^2 using a Caver Lab Press Model C. The container was then fitted with a DF 191 Stainless Steel Cutting Blade and driven by a Sayton Model 4Z538A adjustable speed motor. Compressed air was supplied to the dust generator at 28 psi. The aerosolized dust was then fed directly into the chamber through the dust outlet assembly.

Chamber Concentration Measurements Gravimetric samples were withdrawn on 7 occasions from the breathing zone of the animals. Samples were collected using 25 mm glass fiber filters (GF/B Whatman) in filter holders attached by 1/4 inch tygon tubing to a General Electric Vacuum pump Model 5KH10GGR28. Filter papers were weighed before and after collection to determine the mass collected. The collections were carried out for 2 minutes at air flows of 2 lpm.

Particle Size Distribution An eight-stage Andersen cascade impactor was used to assess the particle size distribution of the test atmosphere. The aerodynamic mass median diameter and geometric standard deviation were determined graphically using two-cycle logarithmic probit axes.

Air Flow Calibration Flow meters for generation and sampling lines were calibrated using a TSI Model 2013 pressure transducer and Model 67 digital linearizer. Chamber air flow was monitored throughout the exposure period and recorded periodically. The air flow varied between 60.3 and 60.8 with the mean of 60.6 lpm.

Exposure Period The exposure period was 4 1/2 hours and the times for 90 and 99% equilibration of the chamber atmosphere were 3.8 and 7.6 minutes, respectively. At the end of the exposure period, the generation was terminated and the chamber was operated for a further 30 minutes thereafter through exposure termination. On removal from the chamber, the animals were individually examined at least once daily for 14 days."

Results:

"No mortalities occurred as a result of exposure. The gravimetric chamber concentration was 2.02 ± 0.15 mg/L with approximately 8% of the particles below 1 micron and 50% below 3 microns. The mass median aerodynamic diameter was approximately 3.0 microns." "The nominal chamber concentration (test substance used divided by total air supplied to the chamber during the exposure) was 16.09 mg/L." According to a memorandum (John Whalan & John Redden to Penelope Fenner-Crisp; 2-1-94) EPA's Hazard Evaluation Division recommends an interim guideline to be used in evaluating inhalation toxicity studies to allow for MMAD's of 1-4 microns in an acute study with a limit concentration of 2 mg/l.

Reported Mortality

Exposure Concentration	(NUMBER KILLED/NUMBER TESTED)		
	Males	Females	Combined
2.02 ± 0.15 mg/L (gravimetric chamber concentration)	0/5	0/5	0/10

Symptoms & Gross Necropsy Findings:

"In-chamber animals observations included decreased activity, ocular and nasal discharge, hunched posture and irregular respiration. Upon chamber removal, similar clinical signs persisted in most rats. All affected animals recovered from these symptoms by day 2 and gained weight over the 14 day observation period. One male exhibited alopecia on its head on days 2 through 12. Gross necropsy findings at terminal sacrifice were generally unremarkable. On female had red foci on the surface of its lungs. All animals had red lung discoloration consistent with euthanasia by CO_2 inhalation. All other tissues and organs appeared normal."

DATA REVIEW FOR ACUTE EYE IRRITATION TESTING (§81-4)

Product Manager: Cynthia Giles-Parker
Reviewer: Van M. Seabaugh
MRID No.: 431902-4
Report Date: 2-25-94
Laboratory: Product Safety Labs, 725 Cranbury Road, East Brunswick, N.J.
Report No.: T-2781
Author: Ralph Shapiro, Ph.D.
Report Title: EPA Primary Eye Irritation
Species: New Zealand rabbits
Sex: 3 of each sex
Weight: Not given
Source: Davidson's Mill Farm, S. Brunswick, N.J.
Dosage: 0.1 gram
Test Material: HORMO 4; EPA Reg. 572-336; lot 13233; white powder; pH 5.5.
Quality Assurance (40 CFR §160.12): Signed statement submitted.
Summary:

-**Toxicity Category:** III.
-**Classification:** Guideline

Procedure:

The rabbits were pre-screened with fluorescein (fls) stain approximately 2 hours before the test. One drop of 2% fls was instilled into both eyes of each rabbit, and then irrigated 30 second later with 30 ml of 0.9% sodium chloride to eliminate rabbits with possible pre-existing ocular defects.

The right eye of each of six rabbits received .1 g of the test substance instilled into the conjunctival sac, and the lids were held together for approximately 1 second before the animal (wearing a neck collar) was returned to its cage. The contralateral eye served as a control. Observations were for 1, 24, 48, 72 hours, and day 4. At the 24-hour observation, fls was used to help evaluate the extent of corneal opacity.

Results:

Observations	(number "positive"/number tested)				
	Hour	Days			
	1	1	2	3	4
Cornea Opacity	0/6	0/6	0/6	0/6	0/6
Iris	0/6	0/6	0/6	0/6	0/6
Conjunctivae					
Redness	1/6	6/6	6/6	2/6	0/6
Chemosis	5/6	4/6	4/6	0/6	0/6
Discharge	4/6	3/6	1/6	0/6	0/6

Comments:

The lab used a 110 scoring system that EPA does not use. The raw data was used to classify the product into a system that EPA uses.

DATA REVIEW FOR SKIN IRRITATION TESTING (§81-5)

Product Manager: Cynthia Giles-Parker (PM22)
Reviewer: Van M. Seabaugh
MRID No.: 431902-05
Report Date: 2-27-94
Laboratory: Product Safety Labs, 725 Cranbury Road, East Brunswick, N.J.
Report No.: T-2782
Title Of Report: EPA Primary Skin Irritation Test

Author(s): Ralph Shapiro, Ph.D.
Species: New Zealand Rabbits
Sex: 3 males; 3 females.
Weight: Not reported, but should be. For future submissions, the weight of the animals should be reported.
Dosage: .5 g of product moistened with 0.5 ml of distilled water.
Test Material: HORMO Root 4; EPA Reg. No. 572-3336; lot #132333.
Quality Assurance (40 CFR §160.12): Signed statement submitted.

Summary:

1. **The Primary Irritation Index** = 0.1

2. **Toxicity Category:** IV

3. **Classification:** Guideline

Procedure: The backs of six rabbits were clipped free of hair (about 10% of the body surface) approximately 24 hours before the experiment began. "Five-tenths of a gram of the test substance was moistened with 0.5 ml of distilled water and applied to one 6 cm_2 intact dose site on each rabbit. The sites were covered with a semi-occlusive dressing for approximately 4 hours at which time the patches were removed and the sites were wiped clean. The sites were scored for erythema and edema at 30 minutes, 24, 48 and 72 hours after patch removal." "...Each test site was immediately covered with a 2 1/4 x 3 inch adhesive-backed gauze patch which was held in contact with the skin using semi-occlusive 3 inch Micropore tape. Neck collars were placed on each rabbit and the animals were returned to their cages. The neck collars and patches were removed after 4 hours of exposure at which time the test sites were gently wiped clean of any residual test substance using water and a clean towel."

Results:
The primary irritation index based on observations at 1-72 hours was 0.1.

Comments:

The PRS likes for powder products to be placed on the skin site underneath a gauze patch, and then moistened with water or other appropriate solvent. In this case, there would be no exothermic reaction, but with other products there might be one. If so, the PRS would want to see what effect an exothermic reaction would have on the skin.

One Liner: For Acute Toxicity. PC Code: 046701 (IBA) | Test material: EPA Reg. No. 572-336
Current Date: 9-21-94

Study/Species/Lab/ Study#/Date	MRID No.	Results	Toxicity Category.	Core-Grade
Oral toxicity §81-1/Sprague Dawley rats/Product Safety Labs/T-2780/2-15-94	431902-1	Limit test: 5 g/kg; 5♂, 5♀; 0/10 mortalilty	IV	Guideline
Dermal toxicity §81-2 /Sprague Dawley rats/Product Safety Labs/T-2783	431902-2	Limit test: 2 g/kg; 5♂, 5♀; 0/10 mortality	III	Guideline
Inhalation toxicity §81-3/Sprague Dawley rats/Product Safety Labs/T-2785	421902-3	Limit test; 4 1/2 hr exposure to gravimetric chamber concentration of 2.02 ± 0.15 mg/L. Mortality: 0/10 (5♀,5♂)	III	Guideline
Eye irritation §81-4/ New Zealand rabbits/Product Safety Labs/T-2781	431902-4	No positive scores for opacity or iritis for observations at 1, 24, 48, 72 hours & day 4. Positive scores for conjunctivae (at least one of the 3 measurements) 6/6 for hours 1, 24, 48; 2/6 at 72 hrs.; 0/6 at 4 days. [PRS note: The laboratory should be told to report the animal weights in future submissions].	III	Guideline
Dermal irritation §81-5	431902-5	P.I.I. = 0.1 for 1, 24, 48, & 72 hrs.	IV	Guideline
Dermal sensitization §81-6	--	Study not submitted. Submit data or request waiver.	--	--